

## UNITED STATES DEPARTMENT OF COMMERCE Patent and Trademark Office

ART UNIT

DATE MAILED:

ddress: COMMISSIONER OF PATENTS AND TRADEMARKS

Washington, D.C. 20231

LAHIVE & COCKFIELD 28 STATE STREET BOSTON MA 02109

DOCKETED

Ect. 28,1999 \*\* RESTRICTION REQUIREMENT

<u> എ. 28 2000</u> - ESP/5 MOS

0

Please find below and/or attached an Office communication concerning this application or proceeding.

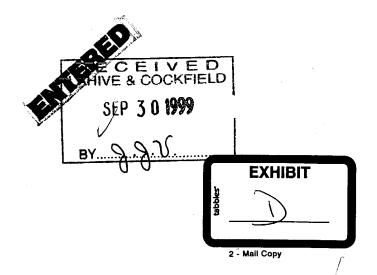
**Commissioner of Patents and Trademarks** 

PECEIVED OCT 27 2004 OFFICE OF PETITIONS

PAPER NUMBER

09/28/99

please se attached



### Office Action Summary

Application No. 09/009,802

Applicant(s)

Examiner

Remy Yucel

Group Art Unit

McCarthy

1636

Responsive to communication(s) filed on Oct 9, 1998	
This action is <b>FINAL</b> .	
Since this application is in condition for allowance except in accordance with the practice under <i>Ex parte Quayle</i> , 19	for formal matters, prosecution as to the merits is closed 335 C.D. 11; 453 O.G. 213.
shortened statutory period for response to this action is ser longer, from the mailing date of this communication. Failure oplication to become abandoned. (35 U.S.C. § 133). Exter 7 CFR 1.136(a).	re to respond within the period for response will cause the
sposition of Claims	
X Claim(s) <u>1-60</u>	is/are pending in the application.
Of the above, claim(s)	is/are withdrawn from consideration.
Claim(s)	
☐ Claim(s)	
Claim(s)	
	are subject to restriction or election requirement.
pplication Papers	1
☐ See the attached Notice of Draftsperson's Patent Draw	ring Review, PTO-948.
☐ The drawing(s) filed onis/are objection	ected to by the Examiner.
☐ The proposed drawing correction, filed on	
☐ The specification is objected to by the Examiner.	
☐ The oath or declaration is objected to by the Examiner.	
iority under 35 U.S.C. § 119	
Acknowledgement is made of a claim for foreign priori	ty under 35 U.S.C. § 119(a)-(d).
☐ All ☐ Some* ☐ None of the CERTIFIED copies	·
☐ received.	
received in Application No. (Series Code/Serial N	lumber)
$\square$ received in this national stage application from t	ne International Bureau (PCT Rule 17.2(a)).
*Certified copies not received:	
Acknowledgement is made of a claim for domestic price	ority under 35 U.S.C. § 119(e).
ttachment(s)	
☐ Notice of References Cited, PTO-892	
☐ Information Disclosure Statement(s), PTO-1449, Paper	No(s)
☐ Interview Summary, PTO-413	
☐ Notice of Draftsperson's Patent Drawing Review, PTO-	948
□ Notice of Informal Patent Application, PTO-152  □ Notice to Comply Sequence □ > Localities + Since Real	

Page 2

Art Unit: 1636

#### **DETAILED ACTION**

Claims 1-60 are pending in the application.

#### Specification

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures and the Raw Sequence Listing Error Report.

Since the response appears to be **bona fide**, but through an apparent oversight or inadvertence failed to provide a complete response, applicant is required to complete the response within a time limit of one (1) month from the date of this letter, 37 CFR 1.135(c).

NO EXTENSION OF THIS TIME LIMIT MAY BE GRANTED UNDER EITHER 37 C.F.R. 1.136(a) OR (b), BUT THE STATUTORY PERIOD FOR RESPONSE SET FOR THIS COMMUNICATION MAILED MAY BE EXTENDED UP TO A MAXIMUM OF SIX (6) MONTHS UNDER 37 CFR 1.136.

#### Election/Restriction

Restriction to one of the following inventions is required under 35 U.S.C. 121:

Art Unit: 1636 -

- I. Claims 1-17, drawn to nucleic acids, vectors, host cells and methods of producing CRSP protein, classifiable in class 536, subclass 23.1 and class 435, subclasses 325 and 69.1.
- II. Claims 18 and 19, drawn to a transgenic animal comprising a transgene encodingCRSP, classifiable in class 800, subclass 8.
- III. Claims 20-31, drawn to isolated CRSP proteins and fusion proteins, classifiable in class 530, subclass 350.
- IV. Claims 32-34, drawn to antibodies which specifically bind CRSP, classifiable in class 424, subclass 130.
- V. Claim 38, drawn to a method of modulating a cell-associated activity by
   stimulating CRSP protein activity or expression classifiable in class 435, subclass
   4.
- VI. Claim 40, drawn to a method of modulating a cell-associated activity by inhibiting CRSP protein activity or expression, using anti-sense, classifiable in class 536, subclass 24.5.
- VII. Claim 41, drawn to a method of modulating a cell-associated activity by inhibiting CRSP protein activity or expression, using an antibody, classifiable in class 424, subclass 130.
- VIII. Claim 44, drawn to a method of treating a subject with a small molecule, classifiable in class 514, subclass 1.

Art Unit: 1636

- IX. Claim 45, drawn to a method of treating a subject with a protein, classifiable in class 514, subclass 2.
- X. Claim 46, drawn to a method of treating a subject with a nucleic acid, classifiable in class 514, subclass 44.
- XI. Claims 50, 51 and 55, drawn to method of detecting for the presence of CRSP activity using nucleic acid, classifiable in class 435, subclass 6.
- XII. Claims 52, 53 and 56, drawn to method of detecting for the presence of CRSP activity using antibodies, classifiable in class 435, subclass 7.1.
- XIII. Claim 59, drawn to an assay for detecting a genetic alteration in a cell, classifiable in class 435, subclass 6.
- XIV. Claim 60, drawn to an assay for detecting a genetic alteration in a cell, classifiable in class 435, subclass 91.

Claims 37 and 42 are generic to groups V, VI and VII.

Claim 39 is generic to groups VI and VII.

Claims 43, 47 and 48 are generic to groups VIII, IX and X.

Claims 49, 54, and 57 are generic to groups XI and XII.

Claim 58 is generic to groups XIII and XIV.

Election of any one of the groups listed immediately above will result in examination of the corresponding generic claim(s).

Art Unit: 1636

The inventions are distinct, each from the other because of the following reasons:

Inventions of groups I-IV are distinct. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different groups are drawn to chemically and biologically distinct products which are not disclosed as capable of use together. For example, the nucleic acids of group I are distinct from proteins and antibodies and transgenic animals of groups II-IV.

Inventions V-XIV are distinct. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different groups are drawn to distinct methods that do not contain the same steps, the methods are not disclosed as capable of use together and the methods all have different functions. For example, the method of claim V is a method of modulating a cell-associated activity by stimulating CRSP protein activity or expression; whereas the methods of groups VI and VII are drawn to methods of modulating a cell-associated activity by inhibiting CRSP protein activity or expression by using chemically distinct products, specifically, antisense nucleic acids and antibodies. Groups VIII-X are drawn to methods of treating an individual and have different functions and effects from the methods of V-VII. Groups XI and XII are drawn to methods of detecting CRSP protein activity in a biological sample and have different functions and effects from methods of modulating a cellular activity (V-VII) and methods of treating an individual (VIII-X). Finally, groups XIII and

Art Unit: 1636

XIV are drawn to diagnostic methods to detect a genetic alteration and have different functions and effects from methods of modulating a cellular activity (V-VII), methods of treating an individual (VIII-X) and methods of detecting CRSP protein activity in a biological sample (XI and XII).

The product of group I may be used in the distinct methods of groups V, VI, X, XI, XIII and XIV. The product of group II is not disclosed as capable of use with any of the methods of groups V-XIV. The product of group III may be used in the distinct methods of groups VIII and IX and the product of group IV may be used in the distinct methods of groups VIII and XII. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the same product may be used in materially different processes such as methods of modulating a cellular activity and methods of diagnosing a genetic alteration (both are performed with the product of group I). Conversely, a method for modulating a cellular activity may be performed with antisense molecules (group I) or with an antibody or a protein (groups IV and III, respectively). Thus, the instant inventions are distinct.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter and as shown by

Art Unit: 1636

their different classification and because the searches required for the groups are not coextensive, restriction for examination purposes as indicated is proper.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

#### Conclusion

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR § 1.6 (d)). The Group 1600 FAX numbers are (703) 308-4242 or (703) 305-3014. Unofficial faxes may be sent to the examiner at (703) 305-7939. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Remy Yucel, Ph. D. whose telephone number is (703) 305-1998. The examiner can normally be reached on Monday through Fridays from 8:30 am to 5:00 pm.

Art Unit: 1636

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. George Elliott can be reached at (703) 308-4003.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Remy Yucel, Ph. D.

September 27, 1999

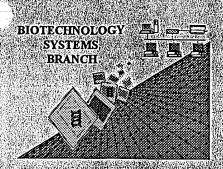
Application No. 09/009802

NOTICE TO COMPLY WITH & QUIREMENTS FOR PATENT APP. ATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 CFR $1.821-1.825$ for the following reason(s):
V 1. This application clearly fails to comply with the requirements of 37 CFR 1.821
- 1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29 May 15, 1990 and at 55 FR 18230, May 1, 1990.
2. This application does not contain, as a separate part of the disclosure on
paper copy, a "Sequence Listing" as required by 37 CFR 1.821(c).
3. A copy of the "Sequence Listing" in computer readable form has not been
submitted as required by 37 CFR 1.821(e).
4. A copy of the "Sequence Listing" in computer readable form has been submitted.
However, the content of the computer readable form does not comply with the requirements of 37 CFR 1.822 and/or 1.823, as indicated on the attached copy of the marked-up "Raw Sequence Listing."
5. The computer readable form that has been filed with this application has been
found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A substitute computer readable form must be submitted as required by 37 CFR 1.825(d).
6. The paper copy of the "Sequence Listing" is not the same as the computer
readable form of the "Sequence Listing" as required by 37 CFR 1.821(e).
7.
Other:
Applicant must provide:
An initial or substitute computer readable form (CRF) copy of the "Sequence
Listing"
An initial or substitute paper copy of the "Sequence Listing", as well as an
amendment directing its entry into the specification
A statement that the content of the paper and computer readable copies are the same
and, where applicable, include no new matter, as required by 37 CFR 1.821(e) or $1.821(f)$ or $1.821(g)$ or $1.825(b)$ or $1.825(d)$
For questions regarding compliance with these requirements, please contact:
For Rules Interpretation, call (703) 308-1123
For CRF submission help, call (703) 308-4212
For PatentIn software help, call (703) 557-0400

# JUG

# RAW SEQUENCE LISTING ERROR REPORT



The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following CRF diskette:

Application Serial Number: 09/09802AArt Unit / Team No. 1636Date Processed by STIC: 9/319

THE ATTACHED PRINTOUT EXPLAINS THE ERRORS DETECTED

PLEASE BE SURE TO FORWARD THIS INFORMATION TO THE APPLICANTS BY EITHER:

- 1) INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE APPLICANTS ALONG WITH A NOTICE TO COMPLY or:
- 2) CALLING APPLICANTS AND CAXING THEM A COPY OF THE PRINTOUT WITH A NOTICE TO COMPLY

THIS WILL INSURE THAT THE NEXT SUBMISSION RECEIVED FROM THEM WILL BE ERROR FREE.

IF YOU HAVE ANY FURTHER QUESTIONS PLEASE CALL

MARK SPENCER 703:308:4212

### Raw Sequence Listing Error Summary

		SUGGESTED CORRECTION SERIAL NUMBER: 09/009 802 A
	ERROR DETECTED	SUGGESTED CORRECTION SERIAL NUMBER: 01/007, 0
ATTN:	: NEW RULES CASES: F Wrapped Nucleics	The number/text at the end of each line "wrapped" down to the next line.  This may occur if your file was retrieved in a word processor after creating it.  Please adjust your right margin to .3, as this will prevent "wrapping".
<del></del>	Wrapped Aminos	The amino acid number/text at the end of each line "wrapped" down to the next line.  This may occur if your file was retrieved in a word processor after creating it.  Please adjust your right margin to .3, as this will prevent "wrapping".
	Incorrect Line Length	The rules require that a line not exceed 72 characters in length. This includes spaces.
	Misaligned Amino Acid Numbering	The numbering under each 5th amino acid is misaligned. This may be caused by the use of tabs between the numbering. It is recommended to delete any tabs and use spacing between the numbers.
	Non-ASCII	This file was not saved in ASCII (DOS) text, as required by the Sequence Rules.  Please ensure your subsequent submission is saved in ASCII text so that it can be processed.
	Variable Length	Sequence(s) contain n's or Xaa's which represented more than one residue.  As per the rules, each n or Xaa can only represent a single residue.  Please-present the maximum number of each residue having variable length and indicate in the (ix) feature section that some may be missing.
	Patentļn ver. 2.0 "bug"	A "bug" in Patentln version 2.0 has caused the <220>-<223> section to be missing from amino acid sequence(s) Normally, Patentln would automatically generate this section from the
	_	previously coded nucleic acid sequence. Please manually copy the relevant <220>-<223> section to the subsequent amino acid sequence.
	Skipped Sequences (OLD RULES)	Sequence(s) missing. If intentional, please use the following format for each skipped sequence:  (2) INFORMATION FOR SEQ ID NO:X:  (i) SEQUENCE CHARACTERISTICS:(Do not insert any headings under "SEQUENCE CHARACTERISTICS")  (xi) SEQUENCE DESCRIPTION:SEQ ID NO:X:  This sequence is intentionally skipped
		Please also adjust the "(iii) NUMBER OF SEQUENCES:" response to include the skipped sequence(s).
1	Skipped Sequences (NEW RULES)	Sequence(s) missing. If intentional, please use the following format for each skipped sequence.  <210> sequence Id number  <400> sequence Id number  000
	Use of n's or Xaa's (NEW RULES)	Use of n's and/or Xaa's have been detected in the Sequence Listing. Use of <220> to <223> is MANDATORY if n's or Xaa's are present. In <220> to <223> section, please explain location of n or Xaa, and which residue n or Xaa represents.
	Use of <213>Organism (NEW RULES)	Sequence(s) are missing this mandatory field or its response.
	(NEW RULES)	Sequence(s) are missing the <220>Feature and associated headings.  Use of <220> to <223> is MANDATORY if <213>ORGANISM is "Artificial" or "Unknown"  Please explain source of genetic material in <220> to <223> section.  (See "Federal Register," 6/01/98, Vol. 63, No. 104, pp. 29631-32) (Sec. 1.823 of new Rules)
	· ·	Please do not use "Copy to Disk" function of Patentin version 2.0. This causes a corrupted file, resulting in missing mandatory numeric identifiers and responses (as indicated on raw sequence listing). Instead, please use "File Manager" or any other means to copy file to floppy disk.  AKS-Biotechnology Systems Branch- 5/15/99

J: Yucel

RAW SEQUENCE LISTING

PATENT APPLICATION US/09/009,802A

DATE: 09/13/1999

TIME: 12:48:44

Input Set: I009802A.RAW

This Raw Listing contains the General Information Section and up to first 5 pages.

supsit

```
<110> APPLICANT: McCarthy, Sean A.
     <120> TITLE OF INVENTION: NOVEL CRSP PROTEIN AND NUCLEIC ACID MOLECULES AND USES
 2
           THEREFOR
 3
     <130> FILE REFERENCE: MEI-008
 4
     <140> CURRENT APPLICATION NUMBER: US/09/009,802A
     <141> CURRENT FILING DATE: 1998-01-20
     <150> EARLIER APPLICATION NUMBER: 08/842,898
 7
                                                                Does Not Comply
     <151> EARLIER FILING DATE: 1997-04-17
                                                           Corrected Diskette Needed
     <150> EARLIER APPLICATION NUMBER: 60/071,589
     <151> EARLIER FILING DATE: 1998-01-15
10
     <160> NUMBER OF SEQ ID NOS: 19
11
     <170> SOFTWARE: PatentIn Ver. 2.0
12
     <210> SEQ ID NO 1
     <211> LENGTH: 2479
14
     <212> TYPE: DNA
16
     <213> ORGANISM: Homo sapiens
     <220> FEATURE:
     <221> NAME/KEY: CDS
18
19
     <222> LOCATION: (38)..(1087)
     <400> SEQUENCE: 1
20
21
           ggcacgaggg ggcggcggct gcggggcgcag agcggag atg cag cgg ctt ggg gcc
                                                    Met Gln Arg Leu Gly Ala
22
23
24
           acc ctg ctg tgc ctg ctg gcg gcg gcg gtc ccc acg gcc ccc gcg
                                                                             103
           Thr Leu Leu Cys Leu Leu Ala Ala Val Pro Thr Ala Pro Ala
26
                                            15
27
           ccc gct ccg acg gcg acc tcg gct cca gtc aag ccc ggc ccg gct ctc
           Pro Ala Pro Thr Ala Thr Ser Ala Pro Val Lys Pro Gly Pro Ala Leu
28
29
                                        30
           age tac ceg cag gag gac acc etc aat gag atg tte ege gag gtt
30
           Ser Tyr Pro Gln Glu Glu Ala Thr Leu Asn Glu Met Phe Arg Glu Val
32
                40
                                    45
33
           gag gaa ctg atg gag gac acg cag cac aaa ttg cgc agc gcg gtg gaa
           Glu Glu Leu Met Glu Asp Thr Gln His Lys Leu Arg Ser Ala Val Glu
34
35
           gag atg gag gca gaa gaa gct gct gct aaa gca tca tca gaa gtg aac
                                                                             295
36
37
          Glu Met Glu Ala Glu Glu Ala Ala Lys Ala Ser Ser Glu Val Asn
38
                            75
                                                80
           ctg gca aac tta cct ccc agc tat cac aat gag acc aac aca gac acg
39
          Leu Ala Asn Leu Pro Pro Ser Tyr His Asn Glu Thr Asn Thr Asp Thr
40
41
                        90
                                            95
          aac gtt gga aat aat acc atc cat gtg cac cga gaa att cac aag ata
42
          Asn Val Gly Asn Asn Thr Ile His Val His Arg Glu Ile His Lys Ile
43
44
                   105
                                       110
                                                           115
```

RAW SEQUENCE LISTING
PATENT APPLICATION US/09/009,802A DATE: 09/13/1999

TIME: 12:48:44

Input Set: I009802A.RAW

														тир	ב אנ	et:	1009	80ZA.RAW
45		200	220	220	C2C	act	aa s	Caa	a t or	ata	+++	tca	aaa	202	att	ato	aca	439
46																	Thr	439
47		1111	120	71011	02.11	1111	OLY	125	rice	Val	1110	501	130		Vul		T 111	
48		tat		gga	gac	αаа	даа		aσa	agg	agc	cac			atc	atc	gac	487
49						-	-		-		-			-			Asp	107
50		135					140	ψ±1	**** 3	3	501	145					150	
51			gac	t.at.	aaa	aaa		ato	tac	tac	caq			age	tta	саσ	tac	535
52	,							-		_			_			_	Tyr	333
53			E	-1-	1	155			-1-	010	160			501		165	- 1 -	
54		acc	tac	caq	cca			aac	cag	agg		ctc	tac	acc	caa		agt	583
55									Gln									
56			4		170	_		- 4		175			- 1		180			
57		qaq	tqc	tqt	qqa	qac	caq	ctq	tgt	qtc	taa	gat	cac	tac		aaa	atq	631
58			_	_		_		_	Cys	_				-			-	
59			-	185	-	•			190		-	•		195		-		
60		gcc	acc	agg	qqc	agc	aat	ada	acc	atc	tgt	qac	aac	caq	agg	gac	tqc	679
61						_			Thr		_	_		_		-	_	
62			200	_	_			205				-	210		_	_	-	-
63		cag	ccg	ggg	ctg	tgc	tgt	gcc	ttc	cag	aga	ggc	ctg	ctg	ttc	cct	gtg	727
64					-		-	-	Phe	_	_		_	_				
65		215					220				-	225					230	
66		tgc	aca	ccc	ctg	ccc	gtg	gag	ggc	gag	ctt	tgc	cat	gac	ccc.	gcc	agc	775
67	-	Cys	Thr	Pro	Lēu	Pro	Val	Glu	Gly	Glu	Leu	Cys	His	Asp	Pro	Ala	Ser	
68						235					240			,		245		
69		cgg	ctt	ctg	gac	ctc	atc	acc	tgg	gag	cta	gag	cct	gat	gga	gcc	ttg	823
70		Arg	Leu	Leu	Asp	Leu	Ile	Thr	Trp	Glu	Leu	Glu	Pro	Asp	Gly	Ala	Leu	
71					250					255					260			
72		gac	cga	tgc	cct	tgt	gcc	agt	ggc	ctc	ctc	tgc	cag	ccc	cac	agc	cac	871
73		Asp	Arg	Cys	Pro	Cys	Ala	Ser	Gly	Leu	Leu	Cys	Gln	Pro	His	Ser	His	
74				265					270					275				
75		agc	ctg	gtg	tat	gtg	tgc	aag	ccg	acc	ttc	gtg	ggg	agc	cgt	gac	caa	919
76		Ser	Leu	Val	Tyr	Val	Cys	Lys	Pro	Thr	Phe	Val	Gly	Ser	Arg	Asp	Gln	
77			280					285					290					
78						_	_		aga		_		_			_	_	967
79		-	Gly	Glu	Ile	Leu		Pro	Arg	Glu	Val		Asp	Glu	Tyr	Glu		
80		295					300					305			-		310	
81									cgc									1015
82		Gly	Ser	Phe	Met		Glu	Val	Arg	Gln		Leu	Glu	Asp	Leu		Arg	
83						315					320					325		
84									ctg									1063
85		Ser	Leu	Thr		GLu	Met	Ala	Leu	-	Glu	Pro	Ala			Ala	Ala	
86					330					335					340			
87			_				-										tgtg	1117
88		Ala			GIĀ	Arg	GIU	Glu	TTE	4 4 6	`d.		10 0	n S	a a sa	hu	mina	y Sheet
89		ma - 1		345				<b>.</b>	350			<i>M</i> (	,	· · · C	/U41			1177
90									_								aggct	
91																	ttgtg	
92													_				gagtc	
93																	tttgc	
94		CCCT	acca	gt t	yyca	ıyaca	ig co	gitt	gttc	tac	atgg	CLE	cgat	aatt	gt t	cgag	gggag	141/

E: 3 RAW SEQUENCE LISTING DATE: 09/13/1999
PATENT APPLICATION US/09/009,802A TIME: 12:48:44

Input Set: I009802A.RAW

```
gagatggaaa caatgtggag tetecetetg attggttttg gggaaatgtg gagaagagtg 1477
 95
 96
            ccctqctttq caaacatcaa cctqqcaaaa atgcaacaaa tgaattttcc acgcagttct 1537
            ttccatgggc ataggtaagc tgtgccttca gctgttgcag atgaaatgtt ctgttcaccc 1597
 97
            tgcattacat gtgtttattc atccagcagt gttgctcagc tcctacctct gtgccagggc 1657
 98
            ageattttea tatecaagat caatteeete teteageaca geetggggag ggggteattg 1717
 99
            ttctcctcqt ccatcaqqqa tttcaqaqqc tcaqaqactq caaqctqctt qcccaaqtca 1777
100
            cacagetagt gaagaccaga geagttteat etggttgtga etetaagete agtgetetet 1837
101
            ccactacccc acaccaqcct tqqtqccacc aaaaqtqctc cccaaaaqqa aqqaqaatqg 1897
102
            gatttttctt ttgaggcatg cacatctgga attaaggtca aactaattct cacatccctc 1957
103
            taaaagtaaa ctactgttag gaacagcagt gttctcacag tgtggggcag ccgtccttct 2017
104
            aatqaaqaca atgatattga cactgtccct ctttggcagt tgcattagta actttgaaag 2077
105
            gtatatgact gagogtagca tacaggttaa cotgoagaaa cagtacttag gtaattgtag 2137
106
            ggcgaggatt ataaatgaaa tttgcaaaat cacttagcag caactgaaga caattatcaa 2197
107
108
            ccacgtggag aaaatcaaac cgagcagggc tgtgtgaaac atggttgtaa tatgcgactg 2257
            cgaacactga actctacgcc actccacaaa tgatgttttc aggtgtcatg gactgttgcc 2317
109
            accatgtatt catccagagt tcttaaagtt taaagttgca catgattgta taagcatgct 2377
110
            ttctttgagt tttaaattat gtataaacat aagttgcatt tagaaatcaa gcataaatca 2437
111
1Ī2
            cttcaactqc taaaaaaaaa aaaaaaaaaa aa
                                                                                2479
      <210> SEQ ID NO 2
113
114
      <211> LENGTH: 350
      <212> TYPE: PRT
115
116
      <213> ORGANISM: Homo sapiens
117
      <400> SEQUENCE: 2
            Met Gln Arq Leu Gly Ala Thr Leu Leu Cys Leu Leu Leu Ala Ala Ala
118
119
                                                  10
120
            Val Pro Thr Ala Pro Ala Pro Ala Pro Thr Ala Thr Ser Ala Pro Val
121
                                              25
                         20
            Lys Pro Gly Pro Ala Leu Ser Tyr Pro Gln Glu Glu Ala Thr Leu Asn
122
123
                                          40
124
            Glu Met Phe Arg Glu Val Glu Glu Leu Met Glu Asp Thr Gln His Lys
125
                                      55
                                                          60
126
            Leu Arg Ser Ala Val Glu Glu Met Glu Ala Glu Glu Ala Ala Ala Lys
127
                                 70
                                                      7.5
128
            Ala Ser Ser Glu Val Asn Leu Ala Asn Leu Pro Pro Ser Tyr His Asn
129
                                                  90
130
            Glu Thr Asn Thr Asp Thr Asn Val Gly Asn Asn Thr Ile His Val His
                                             105
131
                        100
132
            Arg Glu Ile His Lys Ile Thr Asn Asn Gln Thr Gly Gln Met Val Phe
133
                                         120
            Ser Glu Thr Val Ile Thr Ser Val Gly Asp Glu Glu Gly Arg Arg Ser
134
                                     135
135
                                                         140
136
            His Glu Cys Ile Ile Asp Glu Asp Cys Gly Pro Ser Met Tyr Cys Gln
                                                     155
137
                                150
138
            Phe Ala Ser Phe Gln Tyr Thr Cys Gln Pro Cys Arg Gly Gln Arg Met
139
                            165
                                                 170
140
            Leu Cys Thr Arg Asp Ser Glu Cys Cys Gly Asp Gln Leu Cys Val Trp
                                             185
141
                        180
                                                                 190
            Gly His Cys Thr Lys Met Ala Thr Arg Gly Ser Asn Gly Thr Ile Cys
142
143
                                         200
```

Asp Asn Gln Arg Asp Cys Gln Pro Gly Leu Cys Cys Ala Phe Gln Arg

RAW SEQUENCE LISTING
PATENT APPLICATION US/09/009,802A DATE: 09/13/1999 TIME: 12:48:44 GE:

Input Set: I009802A.RAW

145			210					215					220					
146		Gly	Leu	Leu	Phe	Pro	Val	Cys	Thr	Pro	Leu	Pro	Val	Glu	Gly	Glu	Leu	
147		225					230	_				235			_		240	
148	*	Cys	His	Asp	Pro	Ala	Ser	Arg	Leu	Leu	Asp	Leu	Ile	Thr	Trp	Glu	Leu	
149						245					250					255		
150		Glu	Pro	Asp	Gly	Ala	Leu	Asp	Arg	Cys	Pro	Cys	Ala	Ser	Gly	Leu	Leu	
151					260				_	265		_			270			,
152		Cys	Gln	Pro	His	Ser	His	Ser	Leu	Val	Tyr	Val	Cys	Lys	Pro	Thr	Phe	
153				275					280					285				
154		Val	Gly	Ser	Arg	Asp	Gln	Asp	Gly	Glu	Ile	Leu	Leu	Pro	Arg	Glu	Val	
155			290					295					300					
156		Pro	Asp	Glu	Tyr	Glu	Val	Gly	Ser	Phe	Met	Glu	Glu	Val	Arg	Gln	Glu	
157		305					310					315					320	
158		Leu	Glu	Asp	Leu	Glu	Arg	Ser	Leu	Thr	Glu	Glu	Met	Ala	Leu	Arg	Glu	
159						325					330					335		
160		Pro	Ala	Ala	Ala	Ala	Ala	Ala	Leu	Leu	Gly	Arg	Glu	Glu	Ile			
161					340					345					350			
162	<210>	SEQ	ID 1	NO 3														-
163	<211>	LEN	GTH:	105	0													
164	<212>	TYP	E: Di	AN														
165	<213>	ORG	ANIS	М: Н	omo :	sapi	ens											
166	<220>	FEA'	TURE	:														
167	<221>	NAM	E/KE	Y: C	DS						-				_			
168	<222>	LOC	ATIO	и: (	1)	(105	0)											
169	<400>	SEQ	UENC	E: 3														
170		atg	cag	cgg	ctt	ggg	gcc	acc	ctg	ctg	tgc	ctg	ctg	ctg	gcg	gcg	gcg	48
171		Met	Gln	Arg	Leu	Gly	Ala	Thr	Leu	Leu	Cys	Leu	Leu	Leu	Ala	Ala	Ala	
172		1				5					10				-	15		
173		gtc	ccc	acg	gcc	CCC	gcg	CCC	gct	ccg	acg	gcg	acc	tcg	gct	cca	gtc	96
174		Val	Pro	Thr	Ala	Pro	Ala	Pro	Ala	Pro	Thr	Ala	Thr	Ser	Ala	Pro	Val	
175					20					25					30			
176											cag			_				144
177		Lys	Pro	Gly	Pro	Ala	Leu	Ser	$\mathtt{Tyr}$	Pro	Gln	Glu	Glu	Ala	Thr	Leu	Asn	
178				35					40					45				
179											atg							192
180		Glu		Phe	Arg	Glu	Val		Glu	Leu	Met	Glu	Asp	Thr	Gln	His	Lys	
181			50					55					60					
182											gca							240
183			Arg	Ser	Ala	Val		Glu	Met	Glu	Ala		Glu	Ala	Ala	Ala	_	
184		65					70					75					80	
185											tta			_				288
186		Ala	Ser	Ser	Glu		Asn	Leu	Ala	Asn	Leu	Pro	Pro	Ser	Tyr		Asn	
187	•					85					90					95		
188											aat							336
189		Glu	Thr	Asn		Asp	Thr	Asn	Val		Asn	Asn	Thr	Ile		Val	His	
190					100					105					110			
191						-					cag		-		_	_		384
192		Arg	Glu		His	Lys	Ile	Thr		Asn	Gln	Thr	Gly		Met	Val	Phe	
193				115					120					125				
194		tca	gag	aca	gtt.	atc	aca	tct	gtg	gga	gac	gaa	gaa	ggc	aga	agg	agc	432

DATE: 09/13/1999 RAW SEQUENCE LISTING GE: 5

PATENT APPLICATION US/09/009,802A TIME: 12:48:44

Input Set: I009802A.RAW

														-				
195		Ser	Glu	Thr	Val	Ile	Thr	Ser	Val	Gly	Asp	Glu	Glu	Gly	Arg	Arg	Ser	
196			130					135					140					
197		cac	gag	tgc	atc	atc	gac	gag	gac	tgt	ggg	CCC	agc	atg	tac	tgc	cag	480
198		His	Glu	Cys	Ile	Ile	Asp	Glu	Asp	Cys	Gly	Pro	Ser	Met	Tyr	Cys,	Gln	
199		145					150					155					160	
200		ttt	gcc	agc	ttc	cag	tac	acc	tgc	cag	cca	tgc	cgg	ggc	cag	agg	atg	528
201		Phe	Ala	Ser	Phe	Gln	Tyr	Thr	Cys	Gln	Pro	Cys	Arg	Gly	Gln	Arg	Met	
202	,					165					170					175		
203			_						tgc									576
204		Leu	Cys	Thr	_	Asp	Ser	Glu	Cys	_	Gly	Asp	Gln	Leu		Val	Trp	
205					180					185					190			
206									acc									624
207		Gly	His	_	Thr	Lys	Met	Ala	Thr	Arg	GIY	Ser	Asn		Thr	IIe	Cys	
208				195					200				4	205				680
209									ccg									672
210		Asp		GIn	Arg	Asp	Cys		Pro	GIY	ьeu	Cys	220	Ala	Pne	GIII	Arg	
211			210					215							~~~	~~~	at t	720
212									aca Thr									720
213		225	Leu	Leu	Pne	PLO	230	Cys	1111	PIO	пеп	235	vaı	GIU	СТУ	GIU	240	,
214			ast	a a a	000	aaa		aaa	ctt	cta	a a c		ato	acc	taa	gag		768
215 216									Leu									, 00
217	ē	Cys	nra	- Yab	FIU	245	Ber	Arg	пец	пец	250	ДСЦ	110	1111	111	255		
217		gag	cct	gat	aas		tta	gac	cga	tac		t.at.	acc	agt.	aac		ctc	816
219									Arg									
220		O.L.u	110	p	260			LLDP	5	265		-1-			270			
221		tac	саσ	ccc		agc	cac	age	ctg	ata	tat	ata	tac	aaq	ccq	acc	ttc	864
222		_	_						Leu									
223		4		275					280		-		-	285				
224		gtg	ggg	agc	cgt	gac	caa	gat	ggg	gag	atc	ctg	ctg	ccc	aga	gag	gtc	912
225		Val	Gly	Ser	Arg	Asp	${\tt Gln}$	Asp	Gly	Glu	Ile	Leu	Leu	Pro	Arg	Glu	Val	
226			290					295					300					
227		ccc	gat	gag	tat	gaa	gtt	ggc	agc	ttc	atg	gag	gag	gtg	cgc	cag	gag	960
228		Pro	Asp	$\operatorname{Glu}$	Tyr	Glu	Val	Gly	Ser	Phe	Met	Glu	Glu	Val	Arg	Gln	Glu	
229		305					310					315					320	
230									ctg									1008
231		Leu	Glu	Asp	Leu	Glu	Arg	Ser	Leu	Thr		Glu	Met	Ala	Leu		Glu	
232						325					330			•		335		
233									ctg									1050
234		Pro	Ala	Ala		Ala	Ala	Ala	Leu		Gly	Arg	Glu	Glu				
235					340					345					350			
236	<210>	-						3										
237	<211>																	
238	<212>																	
239	<213>				omo s	apıe	:115											
240 241	<220><221>				ne .						,				•			
241	<221>					170	161											
242	<222> <400>				LZ3).	(/2	, 0 ,											
244	(#UU)				gaga	gacc	ra co	rtact	gage	tar	caar	itta	at.ac	raado	eta f	acto	tgggt	60
	Vater	3 mm	55	,	- J~y°	-5405	,_ 0	,-50	- J ~ J \	5	5			,5	•	٠,٠٠٠)	1 1	. آس
Please h	and/or	Xaa l	nave f	- een d	etecte	d in t	he Sc	quenc	e List	ing.	Picas	e revi	cw th	e		L	r ~)_	<b>L</b>
Sequence	e Listin	g to ci	nsure	that	com	cspon	ding (	xplar	ation	is pr	esente	ed in t	be <	220>	to	90		

Use of n and/or Xna have been detected in the Sequence Listing. Please review the Sequence Listing to ensure that a corresponding explanation is presented in the <220> to <223> fields of each sequence which presents at least one n or Xaa.

VERIFICATION SUMMARY PATENT APPLICATION US/09/009,802A DATE: 09/13/1999

TIME: 12:48:44

Input Set: I009802A.RAW

Original Text e ? Error/Warning

90 W "N" or "Xaa" used: Feature required

caatagaaat agctaattta tttccccang tgtgtgct accccatttn attctagagt cnagaacgca aggatctc 42 W "N" or "Xaa" used: Feature required

87 W Invalid/Missing Amino Acid Numbering